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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/826,472

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09/25/2008

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EXAMINER

DUTT, ADITI

ART UNIT

PAPER NUMBER

1649

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/826,472	Applicant(s) MONJE ET AL.	
	Examiner Aditi Dutt	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/20/2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-5,7,8,13,14 and 21 is/are pending in the application.
- 4a) Of the above claim(s) 7-8,13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-5,14 and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/17/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Claims

1. The amendment filed on 20 June 2008 has been entered into the record and has been fully considered. Claims 1 and 3-5 are amended. Claims 7 and 8 are withdrawn by Applicant as drawn to non-elected matter. New claim 21 is added. Claims 2, 6, 9-12 and 15-20 have been cancelled.
It is noted that claim 13, currently withdrawn by Applicant, was examined in the last Office Action dated 12/31/2007, per Applicant's election of the species "disease" in the response dated 10/5/2007. Since Applicant has not provided any explanation for the withdrawal of claim 13, the claim will be considered in the instant application.

Election/Restrictions

2. Applicant's response to previous Office Action in the reply filed on 6 June 2008 is acknowledged.
3. Claims 1, 3-5, 13-14 and 21, drawn to a method of reducing loss of neurogenesis resulting from neuroinflammation due to irradiation, are being considered for examination in the instant application.
4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on 6 June 2008 have been fully considered.

New grounds of objection and rejection are as follows:

Response to Amendment

Withdrawn objections and/or rejections

6. Upon consideration of the Applicant's amendment, all claim objections and rejections, not reiterated herein have been withdrawn, as overcome by cancellation and/or amendment of claims (6 June 2008).
7. Upon consideration of the amendment to claims, rejection under 35 USC § 112, second paragraph is withdrawn.
8. Upon consideration of the amendment and cancellation of claims, rejection under 35 USC § 102(a), (b) and (e) is withdrawn.
9. Upon consideration of the elected restriction to claims of US application No. 11/473,196 that exclude the claims pending herein, and upon cancellation of the '196 conflicting claims, rejection under 35 USC § 101 double patenting is withdrawn.

New Objection/Rejections

10. Applicant's amendment necessitated the following new ground(s) of rejection and/or objection.

Claim Objections

11. Claim 13 is objected for being in the wrong status. Claim 13 currently has a “withdrawn” status, even though it was examined in the last Office Action (dated 12/31/2007). Appropriate clarification and correction is required.

Claim Rejections - 35 USC § 112-Second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
13. Claim 13 is rejected, as being vague and indefinite because, although claim 13 depends from claim 1, it is not clear whether the inflammation is in response to radiation (as in claim 1) or due to “surgical interventions, injury, or disease” (as in claim 13). A clear nexus between the two claims is not discernible. Claim 13 also fails to further limit the method recited in independent claim 1. Appropriate clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1, 5, 14 and 21, are rejected under 35 U.S.C. 102(b) as clearly anticipated by Wright et al. (US PGPB 20020016327 A1, dated 2/7/02).
15. The claims recite a method of reducing loss of neurogenesis capacity resulting from neuroinflammation due to irradiation in an individual, comprising contacting the individual with non-steroidal anti-inflammatory drug (NSAID), indomethacin subsequent to irradiation (claims 1, 5, 21), wherein the neurogenesis is associated with the central nervous system (claim 14).
16. Wright et al teach the treatment of neurogenic inflammation caused by conditions like radiation induced pain or radiation burns (claims 18, 19), by administration of pharmaceutical compositions comprising NSAIDs, e.g. indomethacin along with other anti-neurogenic inflammatory compounds (para 0012, 0080). The neuroinflammatory effect of ionizing radiation resulting inflammation and gliosis along with activation of macrophages/microglia, thereby inducing CNS injury is well established (Price et al. J Med Primatology 30: 81-87,

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2001). Because the method steps disclosed by Wright et al meet the instant claim limitations, the method described in the reference anticipates the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. Claims 1, 3-5, 13, 14 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sonis et al (US PGPB 20010011097 A1, dated 8/2/01), in view of Ferencik et al. (Bratisl Lek Listy 102(3): 123-32, 2001), as evidenced by Price et al. (J Med Primatology 30: 81-87, 2001).
18. The claims recite a method of reducing loss of neurogenesis capacity resulting from neuroinflammation due to irradiation in an individual, comprising contacting the individual with non-steroidal anti-inflammatory drug (NSAID), indomethacin (claims 1, 21), wherein the neurogenesis is associated with the central nervous system (claims 13, 14). The claims further recite that the inflammation and microbial activation results from cranial ionizing radiation, and the anti-inflammatory agent is contacted prior or subsequent to the irradiation (claims 3-5).

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19. Sonis et al. teach treating, inhibiting or preventing mucositis in the human cancer patient with head and neck tumors (para 0005) undergoing radiation therapy, by administration of different therapeutic agents such as indomethacin (claims 3, 24-26; para 0012). The reference further teaches that the administration is initiated 24 hours prior to the antineoplastic therapy (i.e. radiation) (para 0015) and continuing thereafter during the course of the treatment (para 0044).
20. Sonis et al. do not teach that the effect of NSAID on inflammation in the CNS.
21. Ferencik et al. teach that long-term administration of NSAIDs in subjects with Alzheimer's Disease (AD) and senile dementia, result in a protective effect on the onset of AD and slows down the progression of the disease (abstract; page 128, col 2, para 1; page 129, col 1, paras 2-4). It is a well-established fact that neurodegenerative diseases like AD and dementia are associated with progressive loss of neurogenesis in the central nervous system (page 129, "Evidence of damage in neurons inflicted by inflammatory process in AD").
22. It would have been, therefore, obvious to the person of ordinary skill in the art at the time the claimed invention was made to modify the method of treating neuroinflammation and reducing loss of neurogenesis using indomethacin in neurodegenerative diseases as taught by Ferencik et al, by contacting an individual having radiation induced inflammation with indomethacin as taught by Sonis et al. The person of ordinary skill in the art would have been motivated and

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would have expected success because it is known that ionizing radiation results in extensive neuroinflammation and gliosis along with activation of macrophages/microglia, thereby inducing CNS injury (Price et al. J Med Primatology 30: 81-87, 2001). Furthermore, as stated above NSAID administration results in a protective effect in slowing the progression of inflammatory neurodegenerative diseases like AD.

23. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

24. No claims are allowed.
25. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
26. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.
28. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
29. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
21 September 2008

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649